

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Alexander BURGER, et al.

Title: *Medicament For Preventing or Treating Papilloma Virus-Specific Tumor*

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Examiner: S. Foley

Art Unit: 1648

DECLARATION UNDER 37 C.F.R. §1.132

I, Dr. John Nieland, being duly warned, hereby declare and say that:

1. I am a citizen of The Netherlands residing at Tellhöhe 18, 82131 Stockdorf, Germany.
2. Currently I am the director of research at MediGene AG.
3. I have assisted in the experiments detailed below to study the reduction of tumor size and induction of T cell response in patients who were vaccinated with CVLPs consisting of the HPV 16 L1 Δ E7₁₋₅₅ fusion protein, as compared to patients who were vaccinated with a placebo.

Experimental Method

250 μ g of CVLPs/placebo were vaccinated subcutaneously in a blinded, placebo-controlled study of HPV 16-positive CINII/III patients at 0 weeks and after 2, 6 and 12 weeks. The CVLPs consisted of the HPV 16 L1 Δ E7₁₋₅₅ fusion protein.

Results

A. Analysis of the reduction of size of the lesion after 24 weeks:

	Number of patents	Reduction of size of the lesion $\geq 50\%$	Share in %
Verum 250 µg	11	7	64
Placebo	12	4	33

B. Analysis of the T cell response:

		Anti E7 T cell response		Anti L1 T cell response	
	Number of patients	CTL1	TH1	CTL1	TH1
Verum 250 µg	12	2	6	6	10
Placebo	10	0	3	1	6

Conclusion

The data in experiment A shows that lesions of patients who were vaccinated with CVLPs exhibited a reduction in size. The data in experiment B shows induction of the cytotoxic T lymphocytes and T helper cells, which are responsible for the cellular immune response. Therefore, a clear effect for CVLPs consisting of the HPV 16 L1 Δ E7₁₋₅₅ fusion protein has been shown.

4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 19/12/03



[Dr. John Nieland]